Michele Allegra

Dynamic connectivity clusters reflect progressive learning and fast strategy shifts

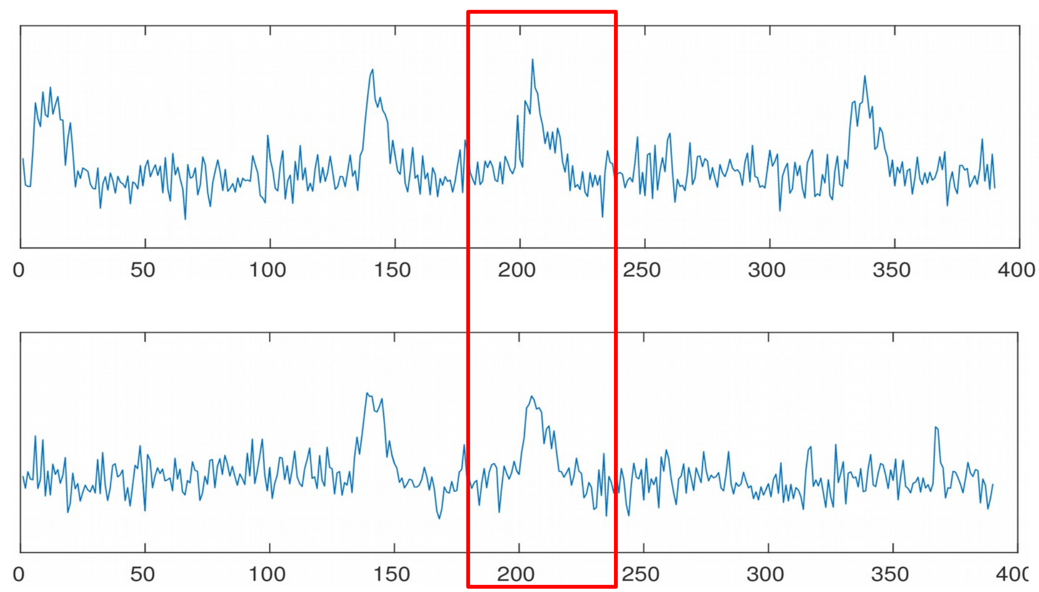
Outline of the talk

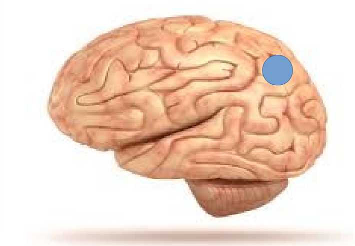
- CDPC: A method to find connectivity clusters in fMRI
    - Density Peak Clustering (DPC): the basics
    - Applying DPC to fMRI: Coherence DPC
- An application of CDPC to a task with two strategies
    - Clustering frequency
    - Effects of learning and strategy-switching

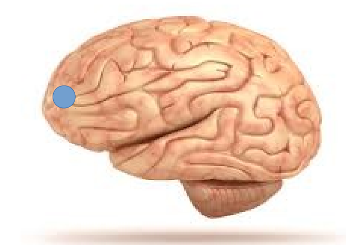
Identifying short-term activity patterns

- **Original idea**: identify brain activity patterns associated to non-
non-repeatable cognitive events

- **Example:** find brain areas co-activated in finding solution of complex problem



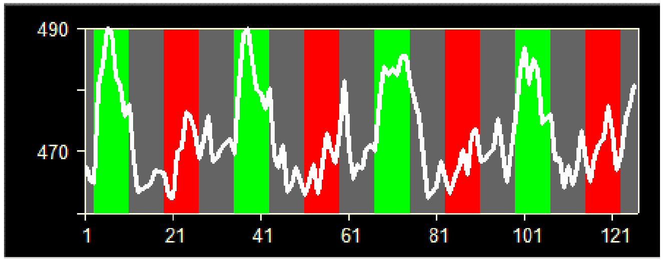




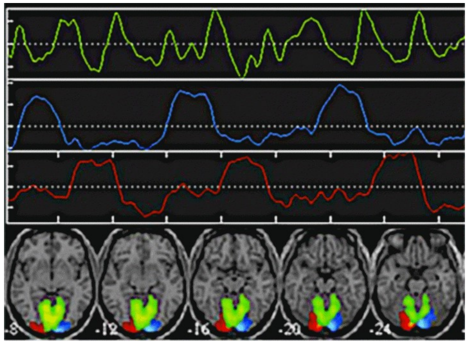
- **Goal:** be able to *identify patterns in fMRI data with high accuracy in short time windows (<30 s)*

Identifying short-term activity patterns

- Supervised methods (GLM) need many repetitions and well-defined model (design matrix)



- Unsupervised methods (ICA) may need long windows for reliable source identification



- **Try Density Peak Clustering**, developed within our group [A Rodriguez, A Laio, Science 344, 1492 (2014)]

- Idea: cluster BOLD time series of different voxels, finding groups of voxels with similar BOLD time-series (connectivity clusters)

DPC(1): density-based clustering

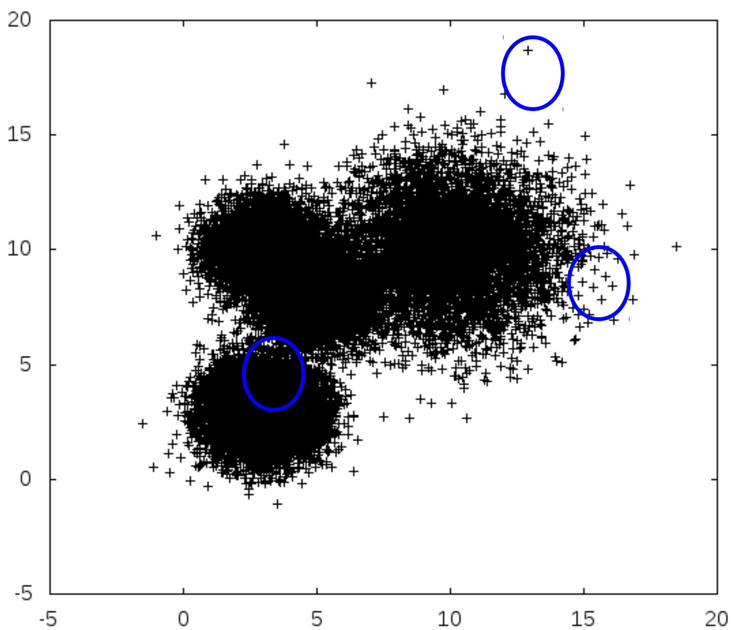
- start from a **metric** d_{ij} that defines distances

- reconstruct **density** around each data point *i*
  [density = probability density from which data are sampled]

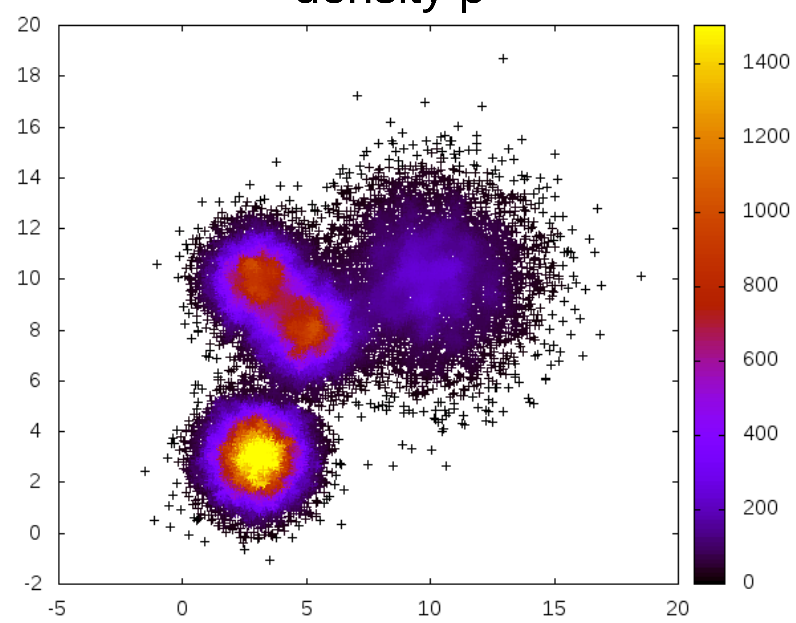
- count # of points in ball or radius ε centered at *i*

$$\rho_i = \sum_{j \neq i} \chi(d_{ij} - \epsilon)$$

$$\chi(a) = \begin{cases} 1 & a \leq 0 \\ 0 & a > 0 \end{cases}$$

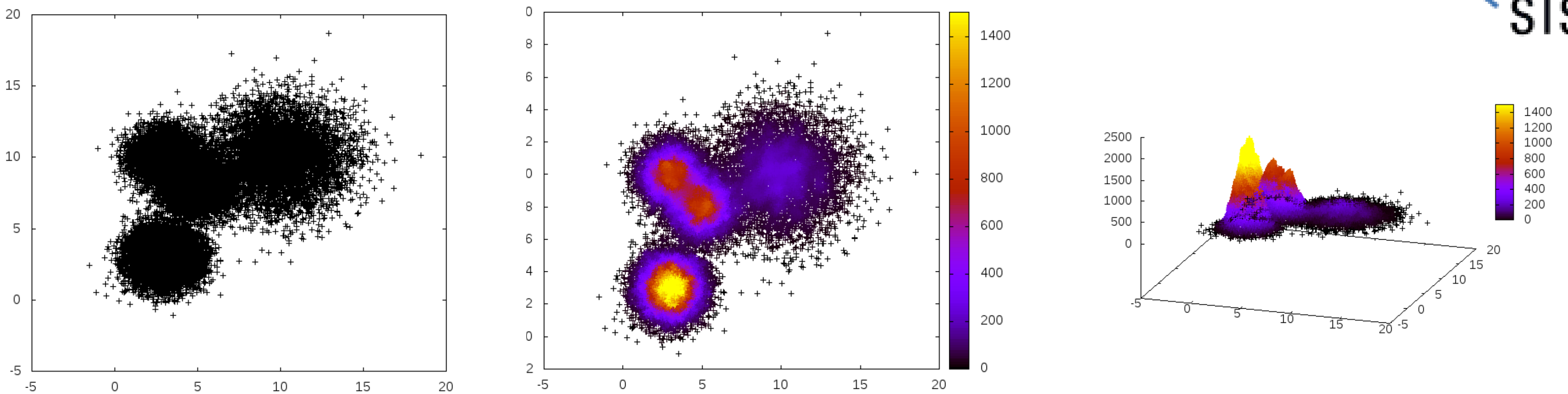


density ρ

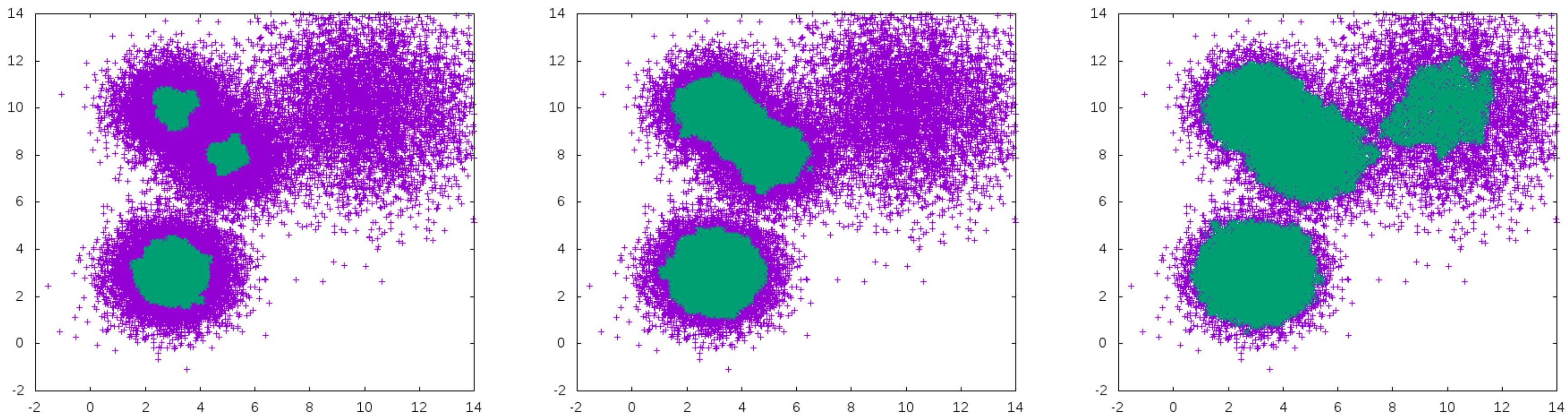


DPC(2): Density-based clustering

- Reconstruct the density



- Standard algorithms (dbscan) identify clusters as disconnected regions of “high density”



- What is high? Results depend on the chosen density threshold!

- Cannot resolve structures at different density scales

DPC (3): finding peaks

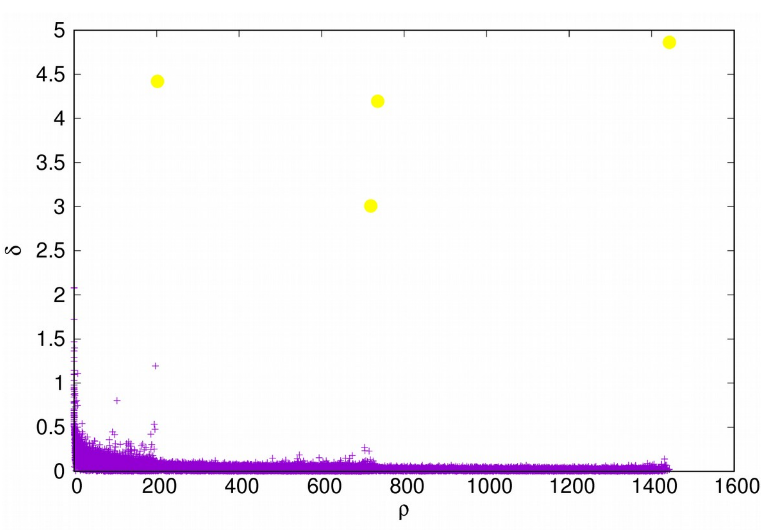
Instead, one can associate a cluster to each density peak

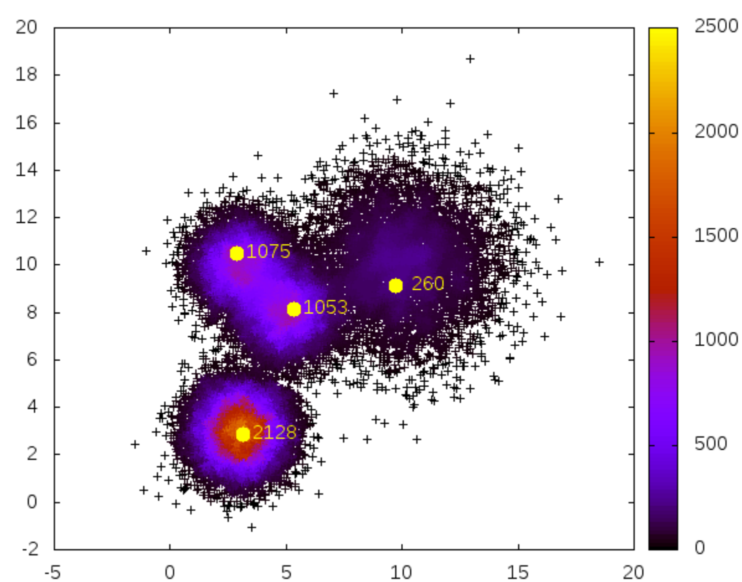
Density peaks are local maxima in the density

Density peaks are far from any point with higher density

Compute for all points min distance from point at higher density $\delta_i = min_{j:\rho_j > \rho_i} d_{ij}$

Peak are outliers in “decision graph” ρ_i vs δ_i :

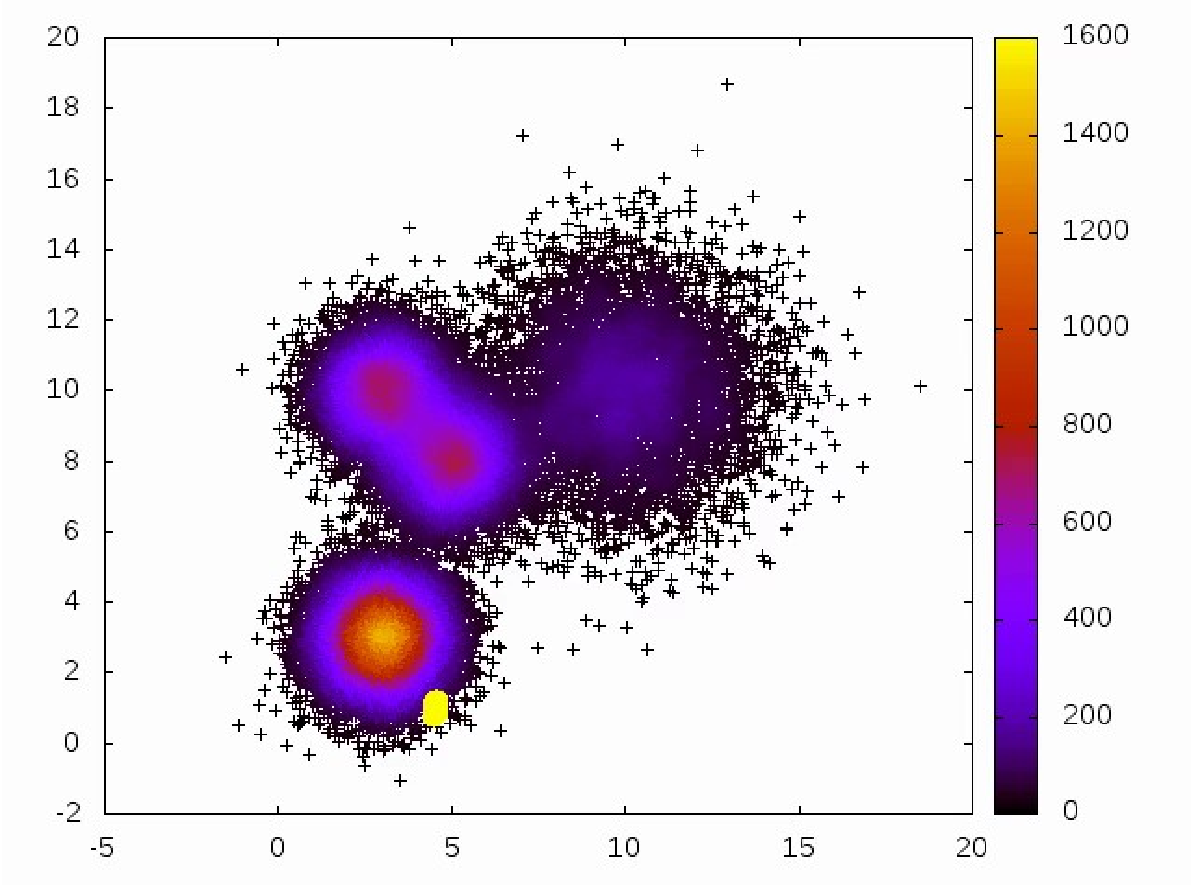




DPC (4): assigning points

Points are assigned to peaks by following a path of increasing density leading to one of the peaks.

Jump from one point to nearest point with higher density

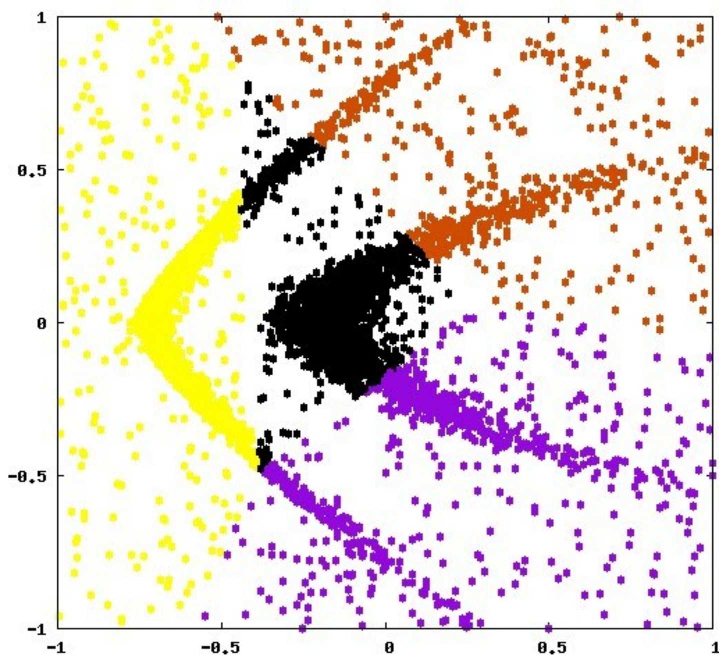


DPC (5): assigning points

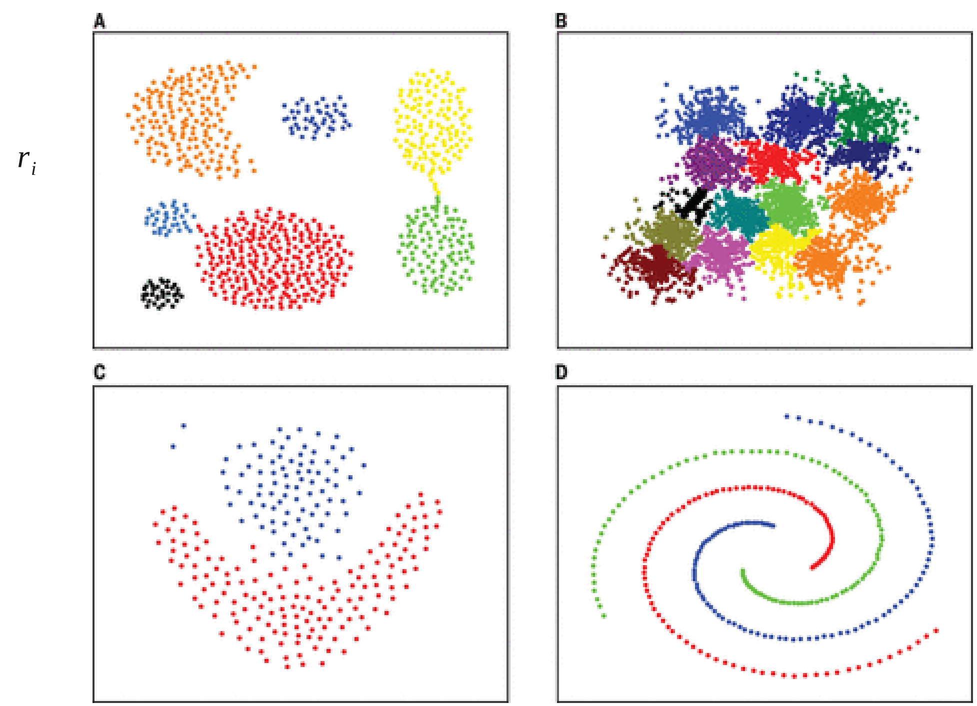
Non density-based clustering methods (e.g. K-means) typically assign point to nearest center, and can only find roughly spherical clusters

Density-based clustering methods allow to retrieve clusters of arbitrary shape

K-means



DPC



DPC (6): pros and cons

Density peak clustering: a new clustering method
[Rodriguez and Laio, Science 2014]

Advantages:

- Computationally cheap (no optimization involved)
- Works well in high dimension (no embedding required, only distances)
- Automatically finds number of relevant clusters
- Finds clusters of arbitrary shape

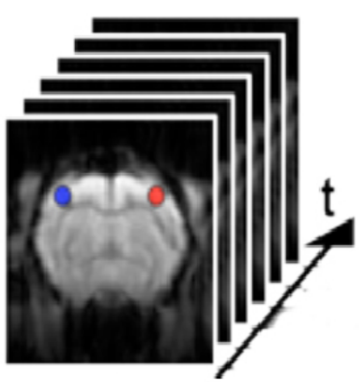
Disadvantages:

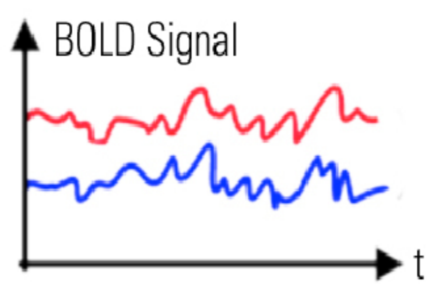
- Requires many data points (>100)
- One free parameter (ε)   [solved in improved version, but higly nontrivial!]

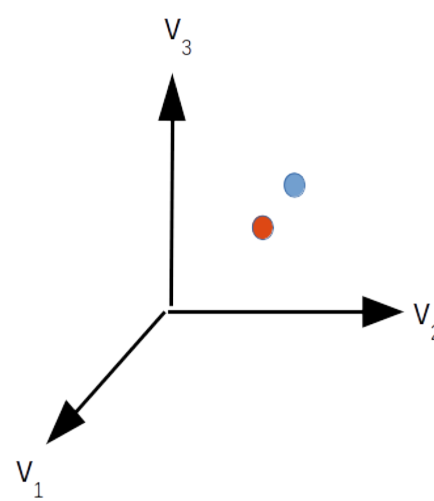
Applying DPC to fMRI

Allegra et al., Hum Brain Mapp 2017

- apply DPC in the space of BOLD time series
- consider window of *T* frames
- to each voxel corresponds a BOLD time series of *T* values, $v_1, v_2, \ldots, v_T$
- consider *T*-dimensional space of time-series
- each voxel time series is a point in this space
- a cluster in this space is group of coherent voxels, i.e. with similar BOLD
- we call such clustering **Coherence Density Peak Clustering (CDPC)**







CDPC: finding a metric

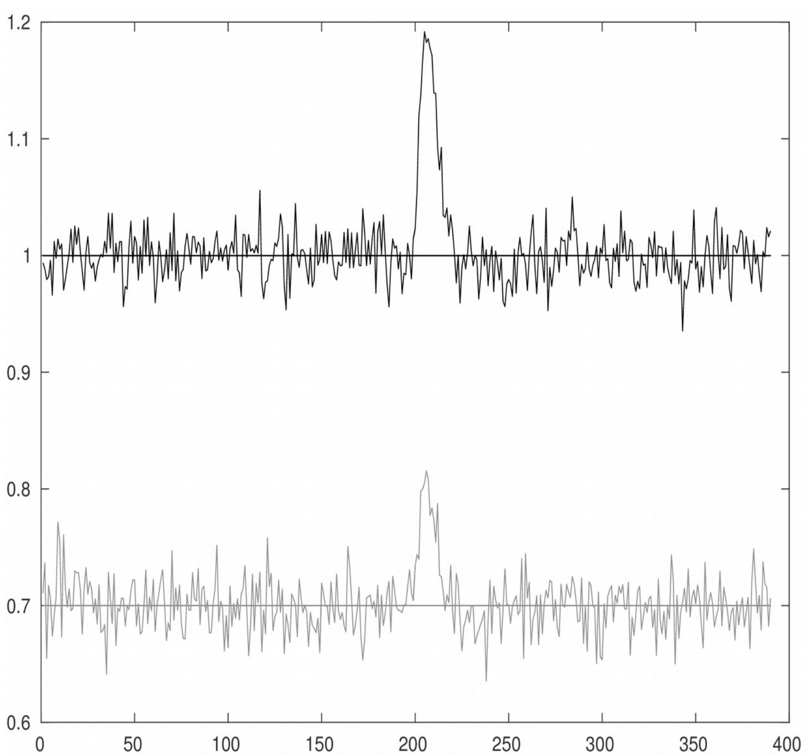
- first, we need a metric d_{ij} to define the distance between BOLD signals of voxels *i* and *j.*

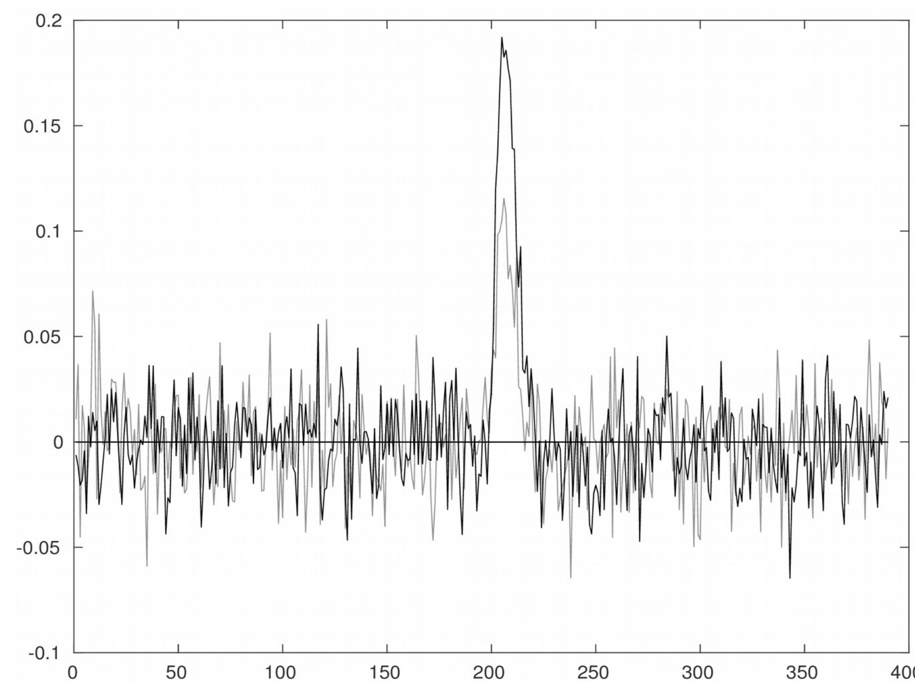
- simplest candidate: Euclidean metric

$$d_{ij} = \sqrt{\sum_t (\nu_i(t) - \nu_j(t))^2}$$

- remove average and normalize amplitude

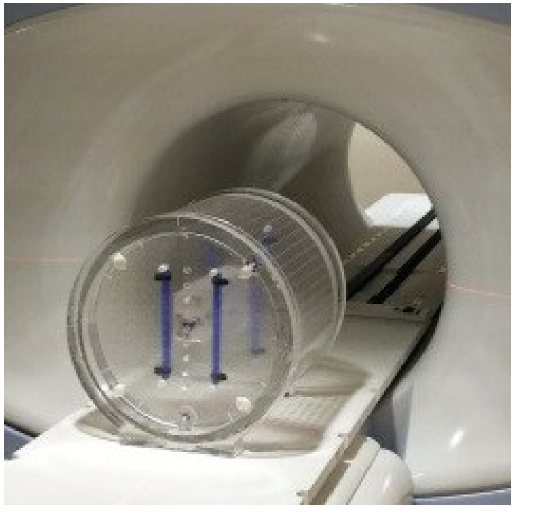
$$d_{ij} = \sqrt{\sum_t (\nu'_i(t) - \nu'_j(t))^2}$$





CDPC: filtering noise

- Where do we “cut” clusters? Can we use a lower threshold on ρ?
- Problem: applying the method on imaging phantom, we find high values of ρ (comparable to real data)
  Noise can be (highly) coherent
- in real images strong coherence between spatially close voxels, in phantom no (sparse coherence)
- Consider small sphere S_i around each voxel *i* and compute “number of coherent neighbor voxels”



$$n_i = \sum_{j \in S_i} \chi(d_{ij} - \epsilon)$$

- n_i is low for phantom, high for real images

CDPC: filtering noise

- Assumption: coherence in a task induces coherence among small (possibly disconnected) regions, not isolated voxels

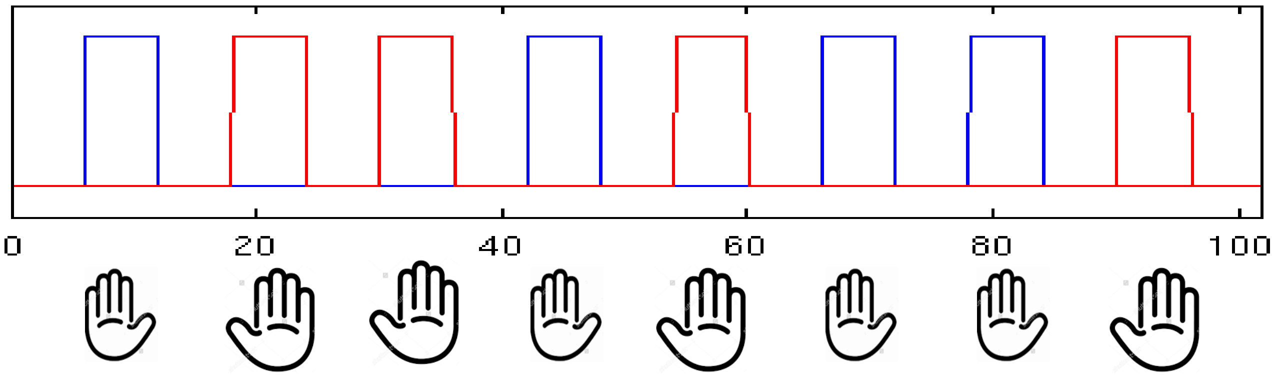
- Let n_0 be max n_i found in phantom: use this as treshold on n_i

- Only voxels with $n_i > n_0$ are considered in the computation of ρ and assigned to clusters

- This (empirical) *noise filter* removes spurious clusters in phantom and simulated data affected by high noise

Simple validation of CDPC: motor experiment

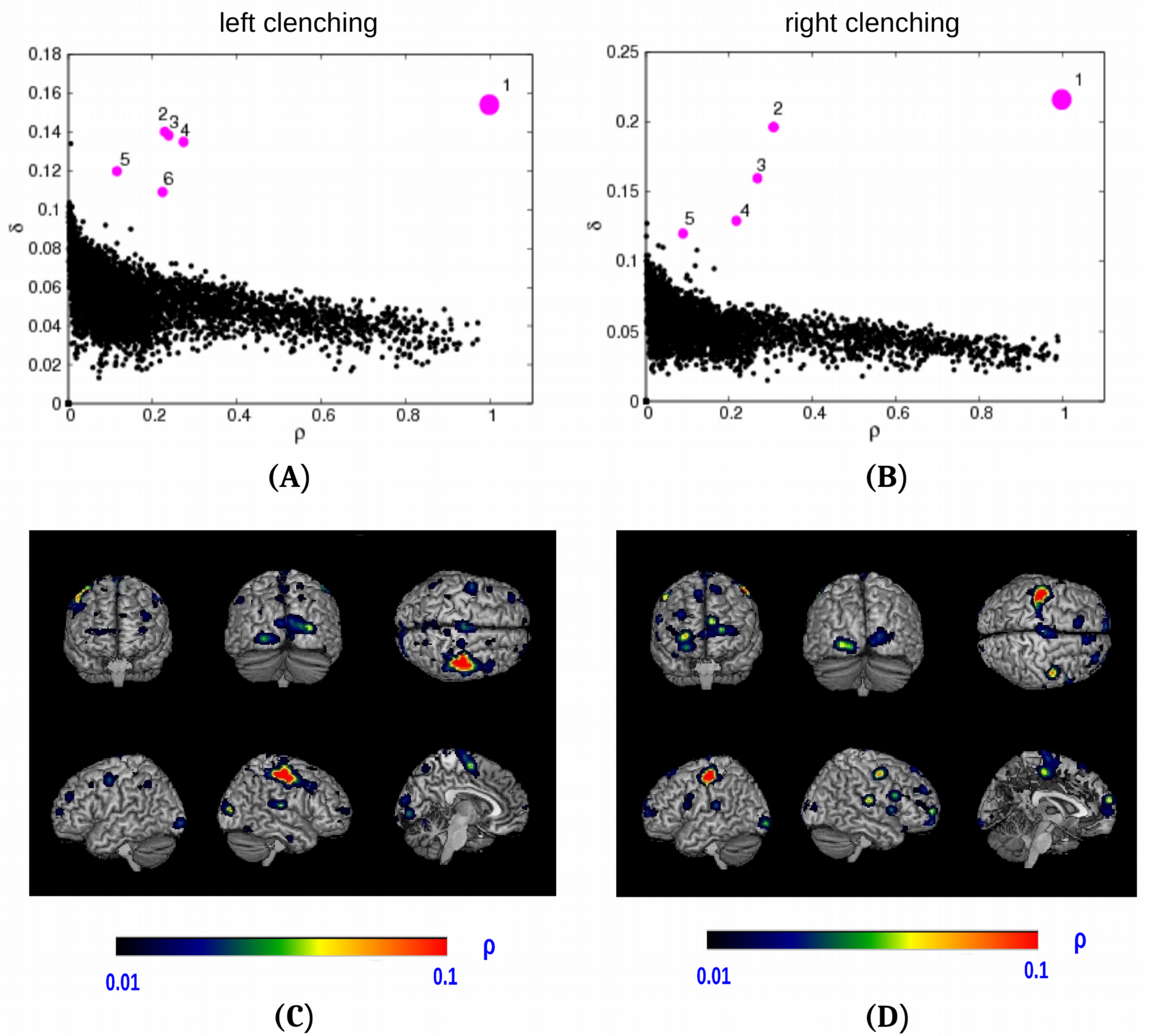
- First test in motor experiment (alternative trials left/right clenching, visually cued)



- Can we reconstruct activity patterns in single trials?

- Apply CDPC to short time windows (~12 volumes, ~20 s) corresponding to single clenching trials

Simple validation of CDPC: motor experiment



In window corresponding to left/right clenching trial we find main cluster including right/left motor cortex

The cluster also includes part of occipital cortex (clenching was visually cued)

Simple validation of CDPC: motor experiment

M. Allegra et al., Hum Brain Mapp 38 (3), 1421 (2017)

Results:

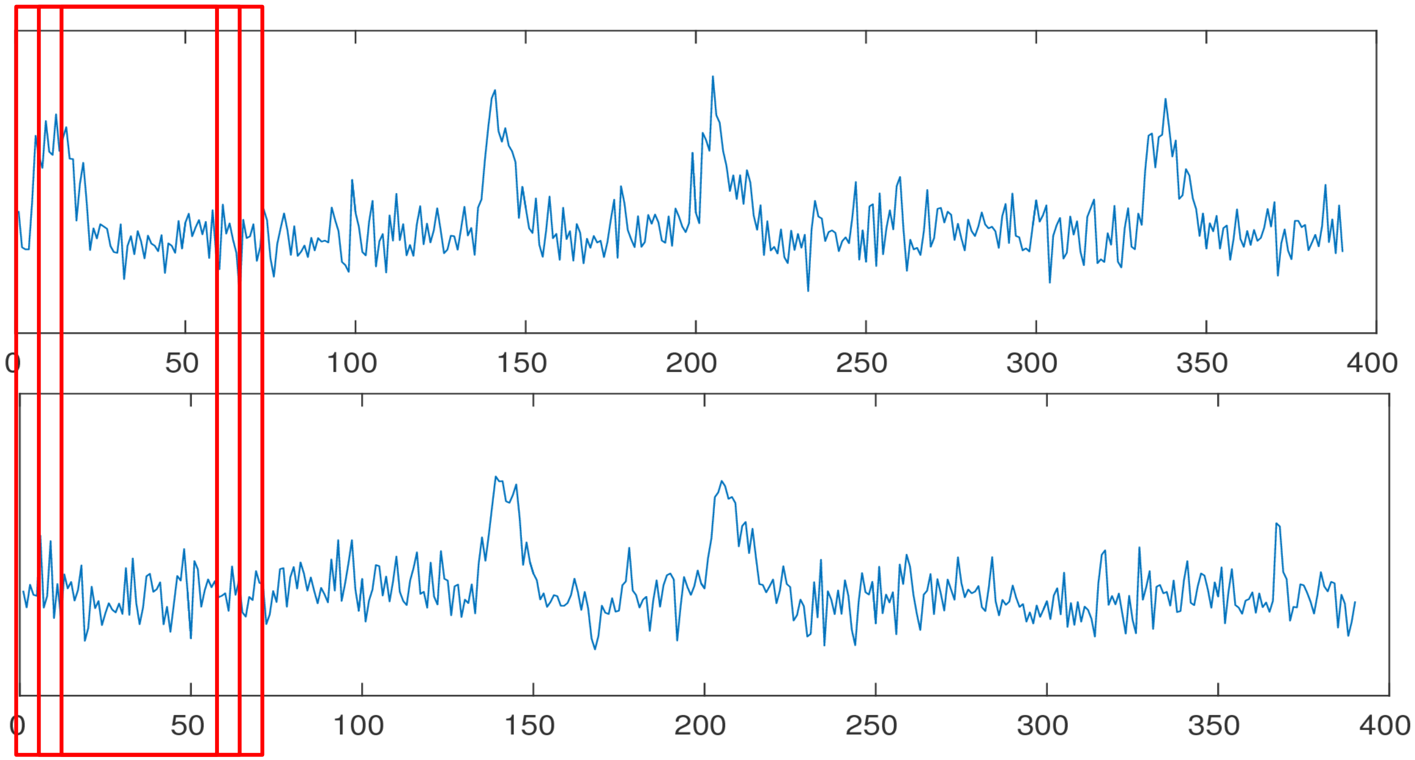
- Proof-of-principle of **coherent pattern detection in single trials**
- Accurate retrieval of coherent patterns, little noise even in single subjects and short time windows
- Results are consistent over subjects

Limitations:

- No null model to perform inference on clustering results
- Two free parameters (n_i and ε)

Many windows together: clustering frequency map

- With CDPC we can in principle retrieve connectivity in single trials
- Looking at several time windows we can track dynamic connectivity in a task
- Apply CDPC on running windows of ~20 s (scans 1-12,2-13,...)



- This allows to detect *transient coherence*, different from global coherence over all windows

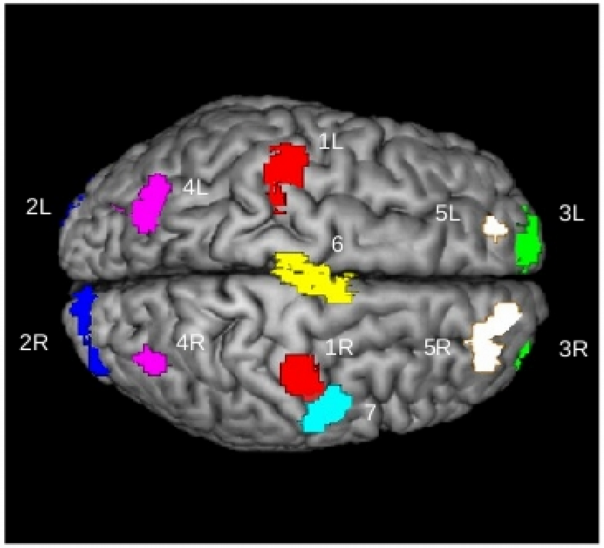
Many windows together: clustering frequency map

- Hypothesis: a brain area participating to the task will be often involved in coherent clusters

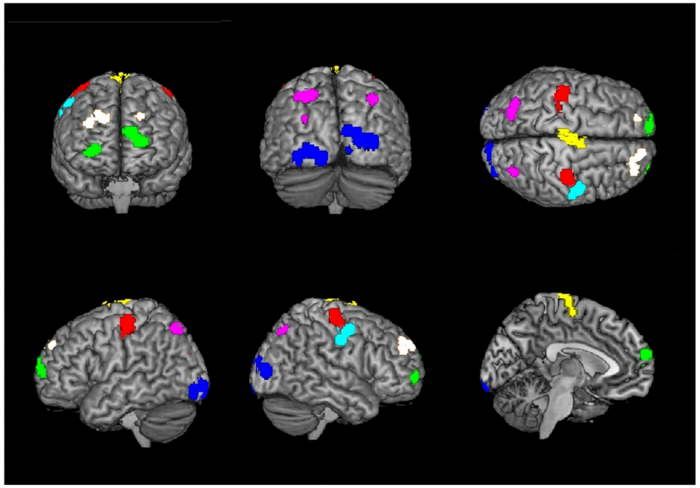
- Put together many windows: Clustering frequency map

windows where voxel *i* is clustered $\Phi_i = \frac{1}{N_t} \sum_t \chi(c_i(t))$

- High-Φ regions for the motor experiment reflect areas involved in the task: motor, parietal, visual, frontal



(A)



(B)

Applying CDPC to more complex experiments

- **Q1**: by means of the clustering frequency map Φ, can we find areas involved in a task?

  If yes, CDPC may be used to find task-relevant areas without supervision

- **Q2:** for a task with several sessions, can we track variations in the functional response by looking at how Φ varies in different sessions?

  If yes, CDPC may be used to track learning and task-switching effects

- **A:** we try to apply CDPC to a task where there is both progressive learning and a sudden behavioral shift,

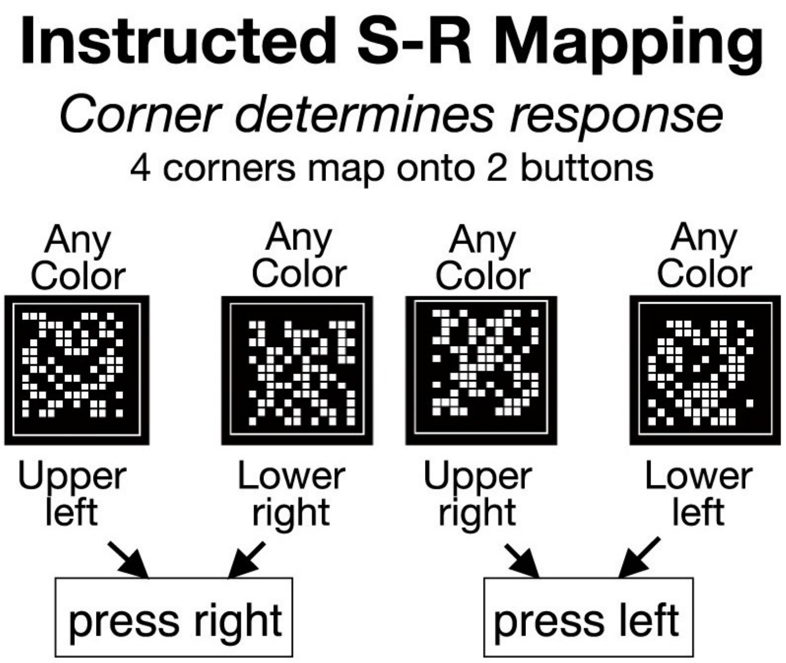
  re-analysis of paper by NW Schuck et al. Neuron 86.1 (2015): 331

A task with two strategies

At each trial, subjects are shown a cloud of dots inside a square

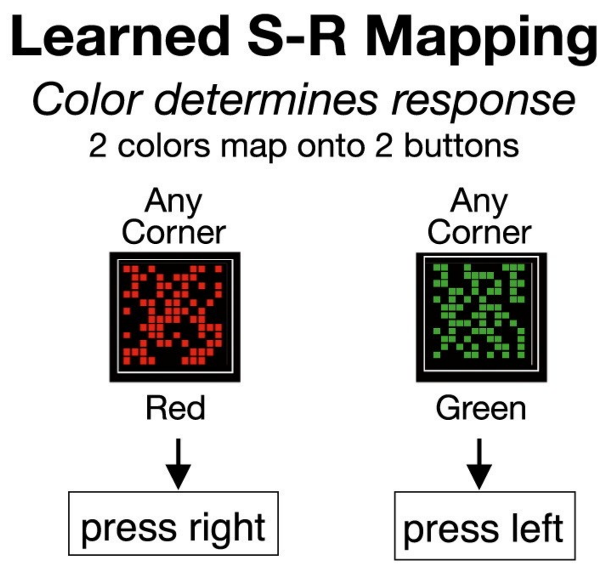
Visual stimulus has **two features**: **corner** (position of dots closer to one corner of the square) and **color** (color of dots, rd or green)

"Judge in which corner of the frame the little squares are.
The squares are colored and can be either red or green"



A task with two strategies

- There are 12 runs of 5 min each; in each run, ~180 trials
- Instructed S-R mapping requires effort: 4-2 mapping, conflict when corner is contralateral to button
- without telling participants, starting from third run a perfect color-corner correlation is introduced, so that UL/LR are always red and UR/LL always green
- Then an alternative, cheaper strategy based on color becomes possible



A task with two strategies

- 11/36 subjects (“**color users**”) spontaneously realize correlation and switch to color strategy in the mid of the experiment

  The switch can be identified with a temporal resolution of 0.5 run (1 block) based on several behavioral markers, e.g. drop in RT, drop in error rate, ...

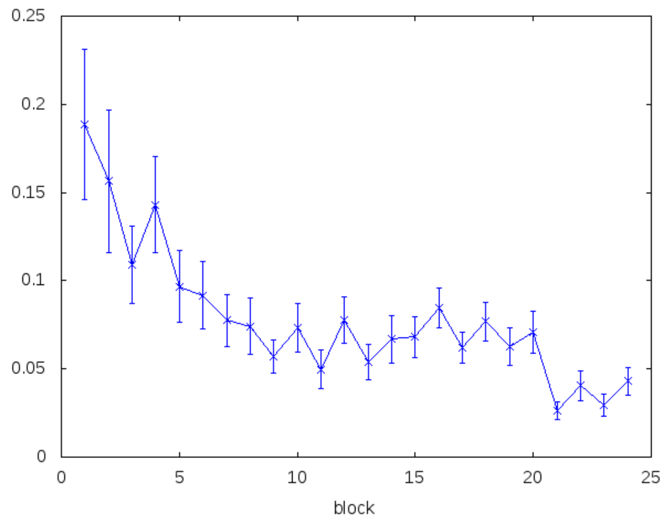
- 25/36 subjects (“**corner users**”) continue to rely on corner information, and are told about the correlation before last two runs

A task with two strategies

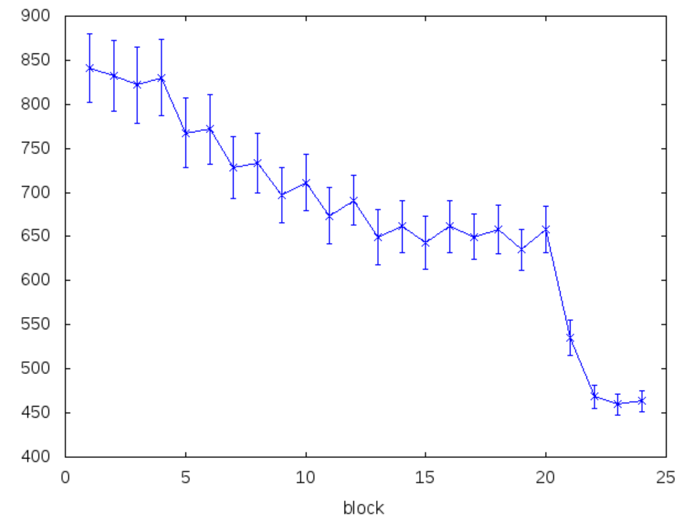
Both color and corner users exhibit learning effects:

- Progressive drop in RT and error rate in corner phase
- Sudden drop in RT and error rate in the (spontaneous or instructed) switch to color phase

error rate



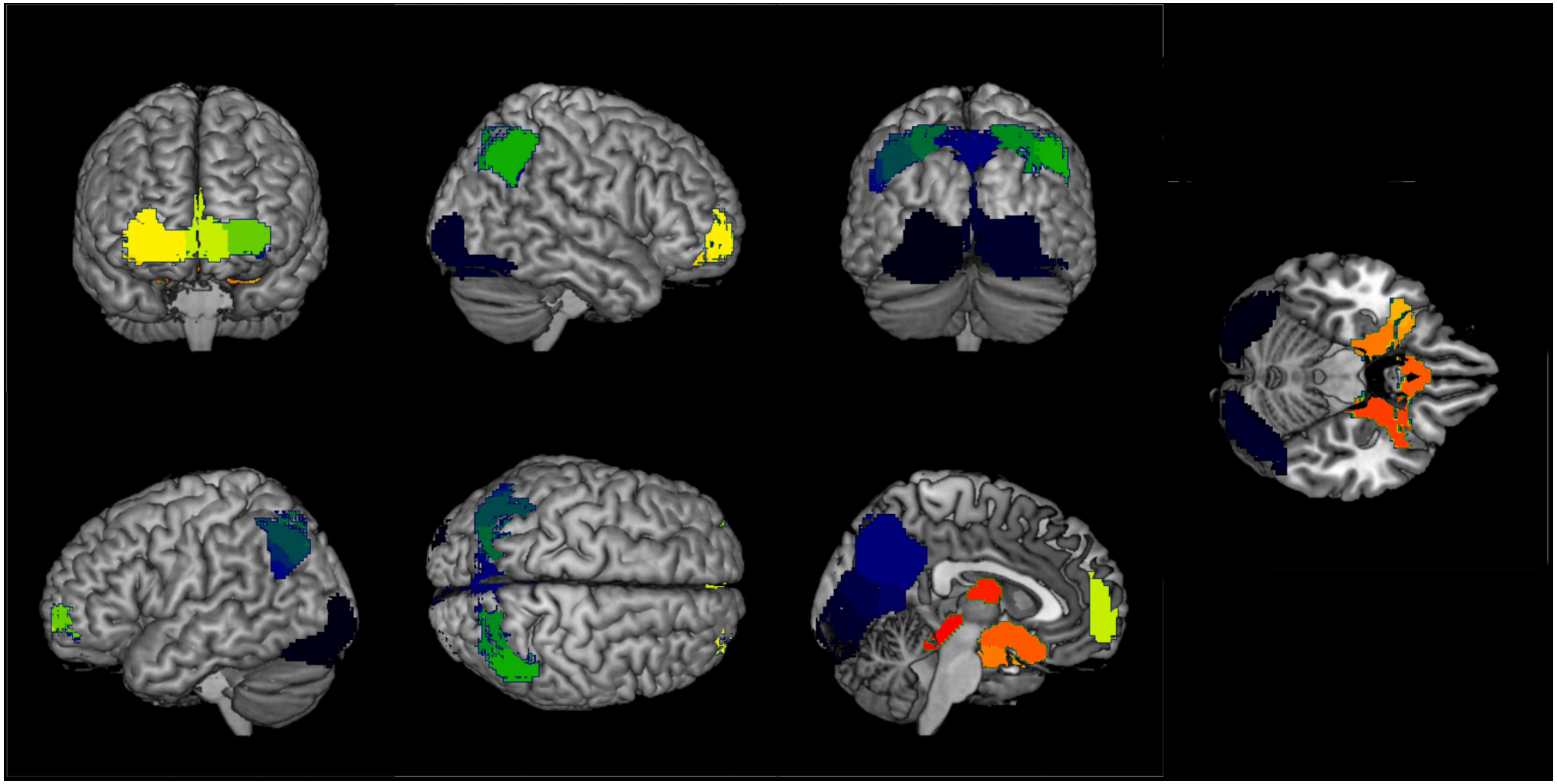
mean reaction times



CDPC results (1): average Φ

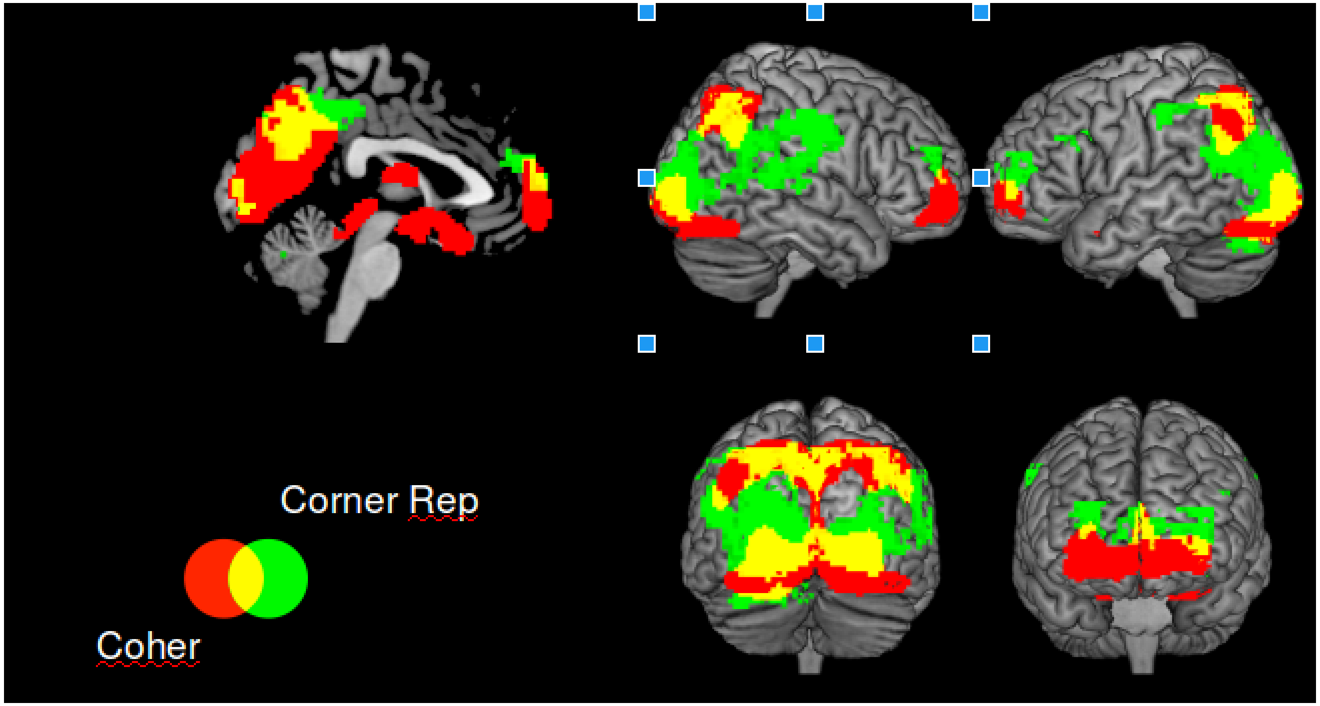
Allegra et al., in preparation (2018)

- we compute Φ for gray matter voxels and use max value found as cutoff for Φ map
- we obtain set of “high-Φ regions” comprising occipital, parietal, and frontal regions, plus deep region in temporal lobe



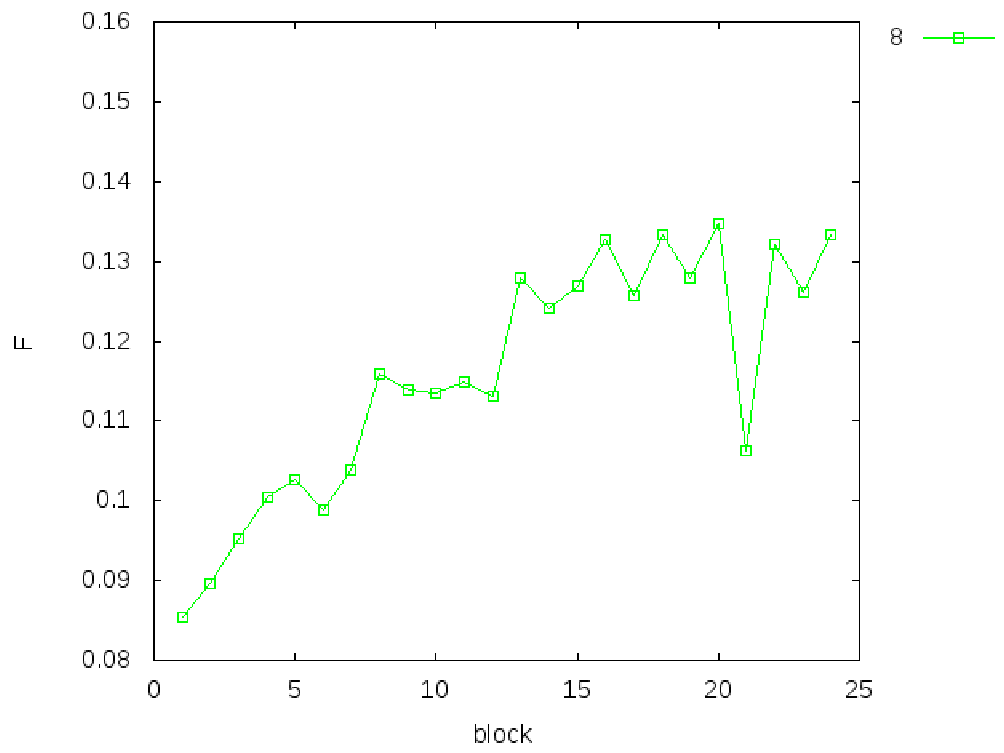
CDPC results (1): average Φ

- Original work (Schuck et al.) focused on corner and color encoding areas (mVPA)
- high-Φ regions (found completely without supervision) largely overlap with regions found by mVPA (highly supervised)



CDPC results (2): changes in Φ

- how does Φ vary with run?
- increase in Φ when subject is performing corner strategy, sudden decrease followed by increase after transition to color

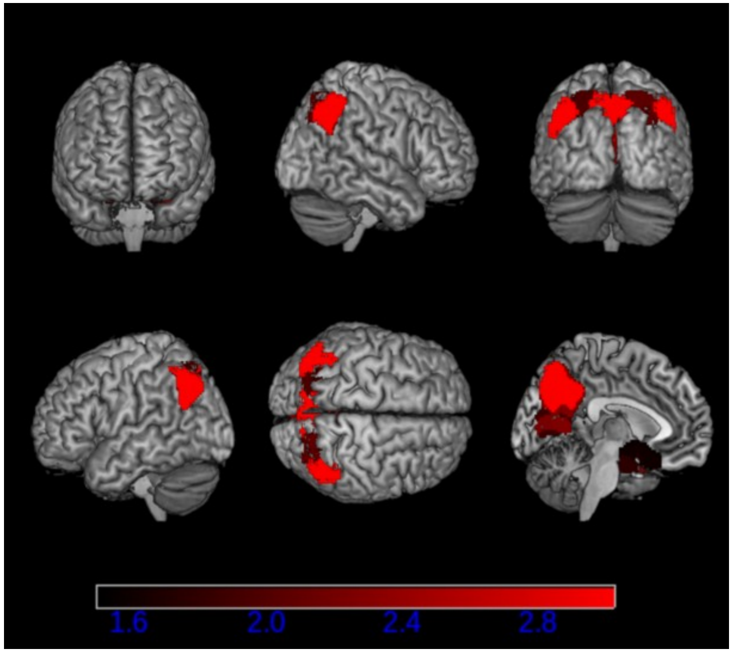


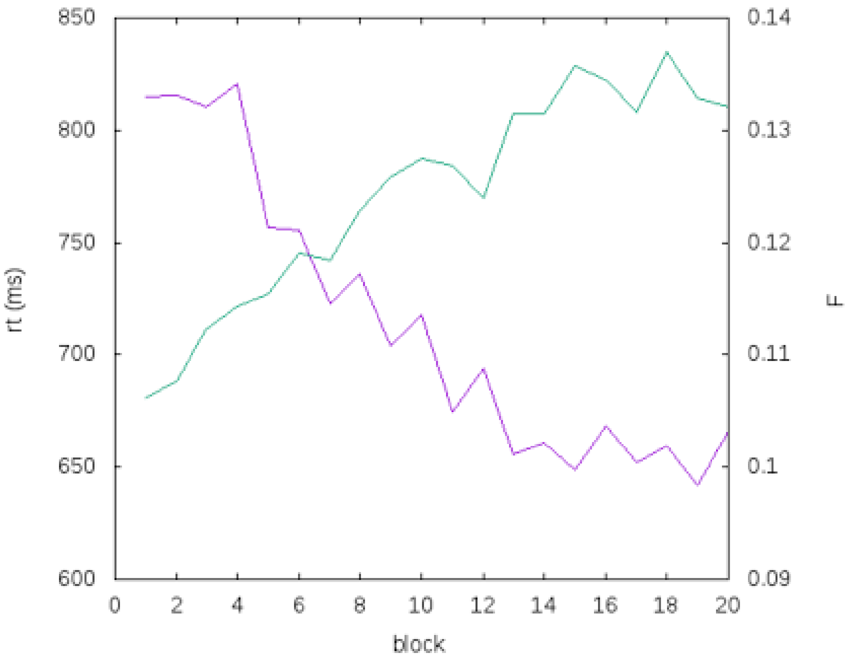
- effect concentrated in parietal cortex and precuneus

CDPC results (2): changes in Φ

- During incremental learning in corner phase, increase in in parietal and precuneus

- Φ increase is correlated with decrease in RT

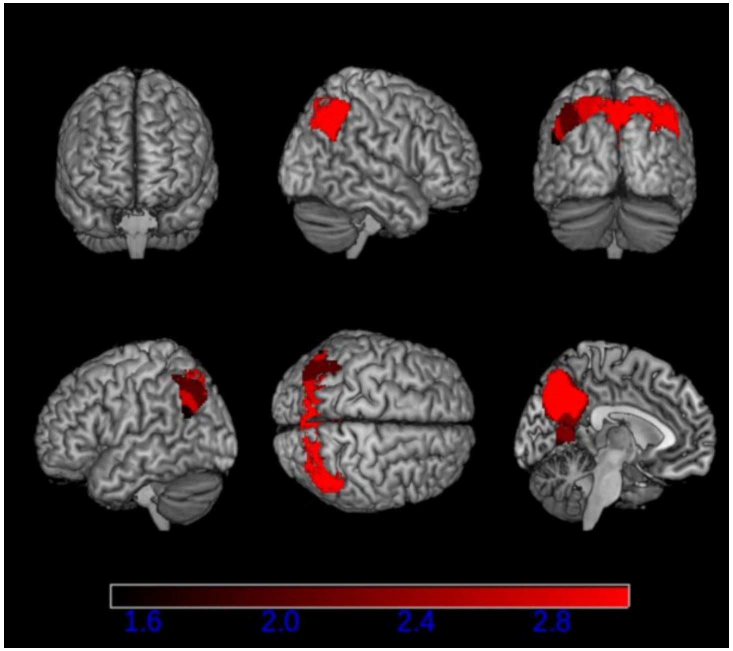




CDPC results (2): changes in Φ

- During instructed switch to color, sudden decrease in Φ in parietal and precuneus

- Same effect in spontaneous switch, although much weaker (lower stats?)



Global summary:

- We developed CDPC, an fMRI analysis method based on the recently introduced Density Peak Clustering
- The method can find groups of voxels with similar activation time series even in sort windows and single subjects
- CDPC can be used with sliding windows approach to find a clustering frequency map (Φ) that represents areas that are recurrently involved in coherent patters in a task
- CDPC is promising tool to find task-relevant regions in fully unsupervised way
- Variations of Φ can be related to incremental learning and sudden behavioral shifts in a task with two strategies
- Task-relevant areas seem to become more synchronized during incremental learning, while such synchronization is disrupted by the strategy change

Acknowledgments

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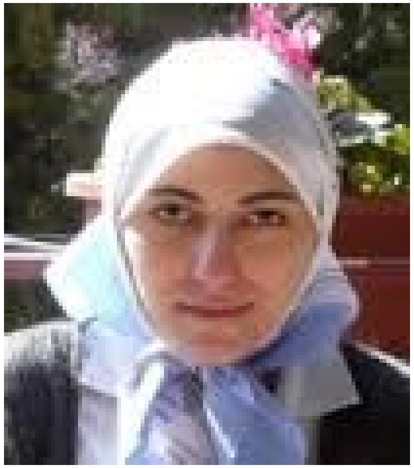

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